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**Single-cell gene expression profiles define self-renewing, pluripotent, and lineage primed States of human pluripotent stem cells.**

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**Public Summary:**

**Scientific Abstract:**

Pluripotent stem cells display significant heterogeneity in gene expression, but whether this diversity is an inherent feature of the pluripotent state remains unknown. Single-cell gene expression analysis in cell subsets defined by surface antigen expression revealed that human embryonic stem cell cultures exist as a continuum of cell states, even under defined conditions that drive self-renewal. The majority of the population expressed canonical pluripotency transcription factors and could differentiate into derivatives of all three germ layers. A minority subpopulation of cells displayed high self-renewal capacity, consistently high transcripts for all pluripotency-related genes studied, and no lineage priming. This subpopulation was characterized by its expression of a particular set of intercellular signaling molecules whose genes shared common regulatory features. Our data support a model of an inherently metastable self-renewing population that gives rise to a continuum of intermediate pluripotent states, which ultimately become primed for lineage specification.

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